To:

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***Notification of discontinuation of a paediatric development which is covered by an agreed PIP Decision***

Gilead Submission Reference: **6624-16-067**

Actives substances(s): Simtuzumab (GS-6624)

Invented name: N/A

Latest Decision number(s): 1) P/0096/2015 2) P/0254/2015

Corresponding PIP number(s): 1) EMEA-001511-PIP02-13 2) EMEA-EMEA-001511-PIP03-14

Please note that development of the medicinal product above in the [condition(s)/indication(s)]:

Treatment of hepatic fibrosis

Treatment of hepatic cirrhosis

Treatment of interstitial pulmonary diseases with fibrosis

☒ has been discontinued

☐ has been suspended/put on long-term hold (with possible re-start at a later time)

for the following reason(s): (tick all that apply)

☒ (possible) lack of efficacy in adults

☐ (possible) lack of efficacy in children

☐ (possible) unsatisfactory safety profile in adults

☐ (possible) unsatisfactory safety profile in children

☐ commercial reasons (please specify: )

☐ manufacturing / quality problems

☐ other regulatory action (please specify: ) (e.g. suspension, revocation of M.A.)

☐ other reason (please specify: )

Please add a brief description (max 2000 characters) of the reason(s) for the discontinuation / suspension:

A meeting of the Data Monitoring Committee (DMC) for Studies GS-US-321-0105 and GS-US-321-0106 was held on 28 October 2016 to review the results of the Week 96 interim analysis. The primary efficacy analyses were not statistically significant for either of these non-alcoholic steatohepatitis (NASH) studies. Based on the recommendation of the DMC, Gilead has opted to terminate the NASH studies due to lack of efficacy.

Gilead has also conducted the primary efficacy analysis for Study GS-US-321-0102 of simtuzumab in patients with Primary Sclerosing Cholangitis (PSC). The primary analysis compared the mean change

from baseline in morphometric quantitative collagen (MQC) between simtuzumab and placebo-treated subjects. Unfortunately this endpoint was not statistically significant, nor were the other secondary endpoints including changes in fibrosis stage and the proportion of subjects that developed liver-related clinical events. No safety concerns were noted. Based on lack of efficacy, Gilead has decided to stop further development of simtuzumab in PSC.

An independent DMC has also completed a review of a prespecified internim analysis of data from adult patients with idopathic pulmonary fibrosis (IPF) treated with simtuzimab (Study GS-US-322-0207). The analysis was performed after accrual of 200 Progression Free Survival (PFS) events. The DMC recommended termination of the study on the grounds of lack of efficacy. Gilead Sciences decided to accept the DMC recommendations, and on 06 January 2016 the study was terminated. Gilead has decided to stop further development of simtuzimab in idopathic pulmonary fibrosis.

No safety concerns were noted for any of these studies.

No further development of simtuzumab is planned.

Name and signature of the PIP contact point:

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Date: 03 November 2016

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